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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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09/974,519

10/10/2001

Dhiren R. Thakker

421/32/2

7285

25297 7590 09/21/2007
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EXAMINER

GRAHAM, SHELLEY R

ART UNIT

PAPER NUMBER

1609

MAIL DATE

DELIVERY MODE

09/21/2007

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary

Application No.

09/974,519

Applicant(s)

THAKKER, DHIREN

Examiner

Shelley R. Graham

Art Unit

1609

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on 23 April 2007.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1,6 and 8 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1,6 and 8 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date <u>2</u> pages. | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114.

Status of the Application

Applicant's Amendment submitted with filing of RCE and Applicant's Arguments/Remarks, all filed on 23 April 2007, have been entered and acknowledged.

The previous claim rejection under 35 U.S.C. § 112, first paragraph, for Claims 1, 6 and 8, set forth in the office action mailed 22 August 2006, is withdrawn in view of Applicant's amendments and remarks contained in Applicant's arguments/remarks filed on 23 April 2007.

Additionally, the previous claim rejection under 35 U.S.C. § 102(b), for Claims 1 and 6, set forth in the office action mailed 22 August 2006, is withdrawn in view of Applicant's amendments and remarks contained in Applicant's arguments/remarks filed on 23 April 2007.

Claims 1, 6 and 8 are currently pending and examined.

Claim Rejections

Rejection under 35 U.S.C. § 103(a)

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

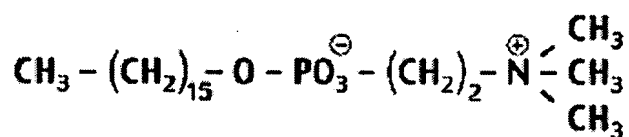
This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

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Claims 1, 6, and 8 are rejected under 35 U.S.C. 103(a) as being unpatentable over Cereijido et al., *Journal of Cell Science*, **1993**, Supplement 17, 127-132 in view of Grunicke et al., *Advan. Enzyme Regul.*, **1996**, 36, 385-407.

Cereijido et al. (page 130: figure 4 and second column, first paragraph) teaches that inhibition of phospholipase C reduces the development of the transepithelial electrical resistance (TER, a measure for the paracellular transport through cells) and activation of phospholipase C increases TER. Thus, one of ordinary skill in the art would understand *a priori* that phospholipase C plays an important role in paracellular transport across the intestinal epithelium and that upon administration of a phospholipase C inhibitor the paracellular membrane permeability would be enhanced.

Grunicke et al. teaches that hexadecylphosphocholine (HePC, Miltefosine, n=15) is an inhibitor of PI-specific phospholipase C (page 393-395, see paragraph beginning with 'The inhibition of PI-specific phospholipase C is a common denominator of all phospholipids analogues').



Examiner would like to point out that it was well known in the art at the time of the invention, that HePC was identified as a prototype of the alkylphosphocholines, and that among the phosphocholines, HePC emerged as one of the most active compounds in the series for the treatment of cancer tumors (Grunicke et al, page 386, second paragraph, lines 6-7). One of ordinary skill in the art, upon a search for a phospholipase C inhibitor in the form of an alkylphosphocholine, would have easily recognized the potential of Miltefosine and its close

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analogues as a phospholipase C inhibitor to enhance paracellular permeability given the teaching of Cereijido in view of Grunicke.

In regards to the formulation of the phospholipase C inhibitor for oral administration, as per Claim 8, it is cited in the instant specification that the formulation and dose preparation techniques are well known in the art. Examiner cites these references as evidence of Applicant's admission to the obviousness of administering orally the invention of the instant application (Oral administration being the route of administration elected by Applicant without traverse in the arguments/remarks submitted on 10 June 2003).

Formulation and dose preparation techniques have been generally described in the art, see for example, those described in U.S. Patent No. 5,326,902 issued to Seipp et al. on July 5, 1994, U.S. Patent No. 5,234,933
25 issued to Marnett et al. on August 10, 1993, and PCT Publication WO 93/25521 of Johnson et al. published December 23, 1993, and each of which is herein incorporated by reference in its entirety.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shelley R. Graham whose telephone number is 571-270-1563. The examiner can normally be reached on M-R 9am-3pm EST.

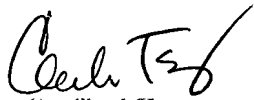
If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin H. Marschel can be reached on 571-272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

SRG

Shelley R. Graham



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